Remarks / Arguments

The only modification to the original responses document was addition of a response to US-PAT-NO: 4,959,228 per the request of the examiner 9/7/01.

Responses to previous patents cited to further show state of the art.

This patent application outlines a process by which a fermentation process can be described. A batch fermentation, like any other chemical process, starts with certain concentrations (mass) of particular chemical species. During the process, these species are consumed and transformed into different chemical species. The quantity of the resulting species (mass) depends on the mass of the starting species.

Because mass is neither created nor destroyed, one mole of carbon that is contained in simple sugars will always be the same mole of carbon after the process. The sugars will be transformed into carbon dioxide and cell biomass. The carbon originally contained in the sugar would, in the end, be contained in carbon dioxide and cell biomass. The important engineering concept of "mass balance" allows one to predict the resulting concentrations of the end products as long as the process is defined adequately.

This patent application outlines a process by which this mass balance can be accomplished for a batch fermentation. The enabling concept of the process is the idea of the cellular yield curve. Microorganisms (cells) transform their substrate (food) differently depending on the type of food it is. In the beginning, the food is consumed quickly. As the food becomes more difficult to utilize, the cells spend more of their resources to process it. Consequently, the cells rate of reproduction decreases. A phase of the batch is approached in which the cells are using all of the energy they acquire from the food to maintain their processes, and no increase in cell mass is observed. Eventually, all of the food is consumed, and the cells start to die off.

The cellular yield curve describes this process for a certain substrate type. This enables a mass balance to be accomplished for the batch. The mass balance specifies the concentrations of the chemical species, and relates all of them to each other. In essence, it describes the entire process.

This precision is much different then a simple statement of how one chemical species is transformed during the process. For example, one could say: sugar is consumed during fermentation, so if the sugar concentration is measured, one can tell when the process is complete. Or, one could say, carbon dioxide is produced during the process, so, when gas production stops, the process is complete. These statements, while true, do not offer one the ability to define the other species involved in the reaction. A mass balance on the system does offer this capability. A mass balance can allow one to say: this 3 grams of consumed sugar has been transformed into 2 grams of carbon dioxide and 1 gram of cell mass. Any method short of the method outlined in this pending patent would not be able to predict the concentrations of all of the related species.

The following patents, generally, fall into the category of measuring a concentration of one of the reacting species. None of them combine measurements in a meaningful way to attain a mass balance of the process. In the following text, the (applied for) patent in question will be referred to as "the pending patent".

US-PAT-NO: 5,900,547

These patents, as a whole, represent different ways to measure specific gravity. As the sugars are consumed during the fermentation, the liquor gets thinner/less dense. This is a symptom of the underling reaction. In the pending patent, the mass balance approach provides the tools to define the system to a precision such that if one reactants' concentration is known, the remaining reactant concentrations can be predicted. If the rate of change of specific gravity is known, the rate of carbon dioxide evolution can be predicted. Conversely, if the carbon dioxide rate is known, the specific gravity can be predicted. It is not a measurement technology, but a modeling methodology. It enables one to develop accurate graphs of the process reactant changes while taking a minimum of measurements. This is sometimes referred to as a "software sensor".

US-PAT-NO: 4,557,186

This invention uses a sensor fitted onto a hydrometer to trigger the discharge of the fermentation liquor into another vessel. It is common in small scale brewing to leave the hydrometer in the liquor. The fermentations usually take place in a glass container, and the progress can be observed by the hydrometer readings. Thus, the only unique feature of this invention is to trigger the removal of the liquor with regard to the action of the hydrometer. One event is triggered The pump is switched on or off.

The pending patent offers a higher degree of resolution than the invention above. Some of the features that it possesses are:

1) Multiple (or no) events can be triggered. Often the liquor is not transferred at a certain stage, but the temperature is lowered.
2) Data from the process can be archived for further study.

Since the entire progress of the fermentation is described, it is as if a hydrometer reading was taken every five minutes for the purpose of compiling a graph. The only data one can obtain from this invention (US-PAT-NO: 4,557,186) is the time the hydrometer triggered the switch. This data is useful, but it does not provide the same resolution as the pending patent.

The only difference between this invention and US-PAT-NO: 4,959,228 is the method of measurement. In US-PAT-NO: 4,959,228, a sound pulse is used

presumably to enable one to assess the condition of the fermentation, and, to trigger a response. This patent (US-PAT-NO: 4,557,186) uses a hydrometer to trigger the pumping of the vessel.

US-PAT-NO: 4,959,228

This invention describes a different approach (or means) to a similar end as the pending patent. The specific gravity is measured (via sound) with the goal of accessing the progress of fermentation. The density (of which specific gravity is a measure) can be correlated to the disappearance of sugar in the solution. However, these inventors have found that this embodiment does "not give useful results" in a fermenting multi-phase beer solution. They have resorted to a mathematical manipulation technique In order to dynamically measure the progress of the fermentation.

This embodiment of the pending patent uses a different means to measure the progress of the fermentation (carbon dioxide evolution). Further, the production/consumption of all of the reactants are predicted. The production/consumption of any of the reactants can be used in place of carbon dioxide evolution to the same end. Carbon dioxide evolves out of the solution, so it is probably the easiest to use.

These inventors (US-PAT-NO: 4,959,228) show that, with their statistical methods, the period of lowest accuracy with their specific gravity method is the middle period. This is because gas evolution compromises the readings. This is the most important part of the fermentation in that during this time, the bulk of the mass conversion activity is occurring. This period also insures good gas evolution, which will result in an excellent evaluation by a carbon dioxide measurement approach.

Additionally, they do not attempt to dynamically describe the concentrations of the reactants.

US-PAT-NO: 3,769,175

This patent relates to fermentation "control" in the physical sense of the word. It makes process changes that increase yeast concentration to decrease the time needed for completion of the fermentation. As a byproduct, the product comes out of the process requiring less additional filtration.

As a side note regarding the utility of the invention, continuous fermentation schemes have never proved reliable for this type of application. It turns out that a small infection of bacteria in the process can quickly compromise the quality of the product. To my knowledge, there is no commercial use of continuous fermentation processes in any brewery in the world, and few if any in other fermentation applications (save waste water).

The pending patent utilizes knowledge of the chemistry of the fermentation (mass balance approach). The approach allows accurate and convenient monitoring of the progression of a fermentation. It is primarily an approach for monitoring; it does not physically alter or change the process in any way.

The opportunities for control come into play when, through an enhanced understanding of the process timing, one decides to physically influence the system. This may be via a temperature change at a certain time, or some other way. One can then monitor the different effects using the methodology in the pending patent. The important point is that no physical alteration of the fermentation process occurs with the pending patent. While this patent physically changes the system to get a different result, the pending patent allows precise monitoring of the system to help look for opportunities for physical control measures. The pending patent is a process, not an apparatus.

US-PAT-NO: 6,150,133

This patent uses a fermentation byproduct as a measure of culture conditions. It does not try to define/characterize the culture's progress. If the byproduct (a conducting acid) is too high, one can back off on substrate additions until conditions improve.

With regard to the RQ (respiratory quotient) discussion, for most of an (anaerobic) fermentation, there is no available oxygen... the container is sealed. Thus RQ does not apply. RQ is used in respirometry to study how materials are degraded. It can also be used in aerobic pharmaceutical fermentations where oxygen is provided. RQ cannot be used to define a fermentation in the way that a properly prepared cellular yield curve can. Nor can RQ be used to define the consumption/production of the reactants in a fermentation.

This patent primarily pertains to a fed batch or continuous operation. Organic acid production is a sign that the microorganisms are either not keeping up with processing the feed, or that there are contaminants in the culture. The presence of organic acids thus signals that the feed rate should be lowered.

Commercial beer brewing is performed as a batch process, thus this invention would not be applicable. This patent is concerning pharmaceutical bioprocesses in which oxygen is provided during the process.

The pending patent helps bring to bear the previously studied/understood characteristics of a fermentation. It does this in the form of the cellular yield curve. It is primarily designed for a straight fermentation, not a fed batch or continuous process. The pending patent methodology could be utilized in such systems to offer a predictive model for comparison to the real time data.

US-PAT-NO: 4,959,228

This patent represents a different means to the same end as the pending patent.

In an effort to follow specific gravity measurements without having to physically take samples, the authors measure the liquor density by the change in the speed that it takes for sound to travel through it. They state that the method works well with a single-phase liquid. This is because the sound measurements in such a solution provide a repeatable, non-variable data set that can then be correlated to a specific gravity value.

A fermentation, however, is a multi-phase environment. At the peak of fermentation, the liquor contains water, ethanol, sugar, yeast (solids), and carbon dioxide bubbles (gas). It is at this condition that the author admits that the technique is not useful.

The question then becomes: how can the technique be extended to overcome this limitation?

One way would be to send a sample through a small whirlpool. The yeast solids would concentrate in the center, and the carbon dioxide gas would be forced to the outside. One could then perform the measurement on the remaining liquor, and make a correlation to the specific gravity. This fix is undesirable because it requires pulling some liquid out of the fermentation. If one is going to do that, then the specific gravity can then be measured directly. This process would also involve a sub system that would harbor bacteria that could contaminate the fermentation if the sample is replaced. If a sample is removed, it should never be reintroduced back into the fermentation batch for hygiene reasons.

The authors, to determine the specific gravity during the peak of the fermentation, use a statistical method. The highly variable data set that is acquired from the sound speed measurements need to be correlated with the actual specific gravity readings beforehand. Then, if the process is repeated in the exact same fashion as before, the correlation would be valid.

What if one wanted to change the batch in some way (i.e. temperature, substrate quality, substrate quantity, etc.)? With this technique, the previous correlation would not be valid. A new set of correlations would have to be generated each time, for each case. This is not practical. This type of requirement would (in my opinion) result in the technique having little value for fermentation process's that need to change conditions often.

The pending patent uses the carbon dioxide evolved as an indicator of specific gravity. The only correlation required beforehand is a yield curve. This yield curve describes how much new yeast mass the yeast (or other microorganism) can gain from each successive fraction of the substrate. As long as the substrate doesn't change appreciably in quality, the technique will allow accurate determination of specific gravity. If one drastically changes substrate quality, then a new yield curve (correlation) should be generated. These yield curves themselves have utility to the operator. They describe the quality of the substrate

so that different substrates (e.g. grains, pre-processing, syrups, etc.) can be compared and assessed.

The technique described in the pending patent allows for further quantification of the materials used as the fermentation media (via the yield curve), and for unobtrusively following the specific gravity. These attributes make it a highly attractive technique for use in fermentation processes that are often varied/changed (such as the beer brewing process).

These are extra copies of the clean (amended) and marked-up (original) drawings.

Please forward to the official draftsperson.

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Remarks / Arguments

These drawings have been extensively modified to comply 37 CFR 1.84. The graphs have been changed to black and white line art, and the tables have been modified to be clearer. Also, the equations have been removed from the specification and included with the drawings. Each entry is properly identified with a "FIG." Preceding the drawing number.